CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-571/S-021

Administrative/Correspondence Reviews

EXCLUSIVITY SUMMARY FOR NDA # 20-571 SUPPL # 021

Trade Name Camptosar® Injection

Generic Name irinotrecan hydrochloride injection

Applicant Name Pfizer Inc HFD # 150

Approval Date If Known June 24, 2004

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES /_X_/ NO /___/

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

SE8

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /_X_/ NO /___/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

Pediatric Exclusivity determination - No efficacy claim is made. The applicant is not recommending the use of irinotecan in children, however they would like to include pediatric information about the pharmacokinetics (PK) and safety of irinotecan in the label. OCPB recommends that information on the PK and safety information in the pediatric population should be included in the label under the PRECAUTIONS section, Pediatric Use subsection.

d) Did the applicant request exclusivity?

YES /__X_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

____6 months_____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /_X_/ NO /___/

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Writen Request?

____Yes_____

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

This is a Pediatric Supplement for an approved product which has been granted 6 months exclusivity effective March 11, 2004 (see Pediatric Exclusivity Determination Checklist in DFS).
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /_X_/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 20-571 _____

NDA# _____ _____

NDA# _____ _____

The same original NDA uses are included in this supplement- no new use.

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.) IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical

investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X_/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /_X_/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

This is a Pediatric Supplement for an approved product which has been granted 6 months exclusivity effective March 11, 2004 (see Pediatric Exclusivity Determination Checklist in DFS). The applicant met all of the requirements of the Written Request. No efficacy claim is made and no labeling changes

have occurred in this regard. The only labeling revision is in PRECAUTIONS, Pediatric Use subsection.

YES /___/ NO /_X_/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /_X_/

If yes, explain:

---

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /_X__/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

The applicant submitted results from 6 studies (listed below) to fulfill the Agency's October 30, 2000 Written Request letter.

Phase I Studies:

1- H6957: A Pediatric Phase I and Pharmacokinetic Study of Irinotecan (Weekly x 4 every 6 weeks) 2- P9571: A Trial of Irinotecan in Children with Solid Tumors (Daily x5 every 3 weeks 3- P9871: A Phase I Study of Irinotecan in Patients with Refractory Solid Tumors who are Concomitantly Receiving Anticonvulsants: A COG Study (Daily x5 every 3 weeks) 4- Saint Jude Children's Research Hospital: A Phase I Study of Irinotecan (CPT- 11) in Pediatric Patients with Refractory Solid Tumors (Daily x5, x2 every 3 weeks)

Phase II Studies:

1- P9761: Phase II Trial of Irinotecan in Children with Refractory Solid Tumors: A POG/ CCG Intergroup Study (Daily x 5 every 3 weeks)

Tumor types: previously treated Ewing's sarcoma/ PNET, neuroblastoma, osteosarcoma, rhabdomyosarcoma, and other extracranial solid tumors; and medulloblastoma, glioma, ependymoma, brain stem glioma, and other CNS tumors

2- D9802: A Phase II "Up- Front Window Study" of Irinotecan (CPT- 11) Followed by Multimodal, Multiagent Therapy for Selected Children and Adolescents with Newly Diagnosed Stage 4/ Clinical Group IV Rhabdomyosarcoma: An IRS- V Study (Daily x 5, x 2 every 3 weeks)
Tumor type: previously untreated rhabdomyosarcoma

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

The applicant submitted results from 6 studies (listed below) to fulfill the Agency's October 30, 2000 Written Request letter.

Phase I Studies:
1- H6957: A Pediatric Phase I and Pharmacokinetic Study of Irinotecan (Weekly x 4 every 6 weeks) 2- P9571: A Trial of Irinotecan in Children with Solid Tumors (Daily x5 every 3 weeks 3- P9871: A Phase I Study of Irinotecan in Patients with Refractory Solid Tumors who are Concomitantly Receiving Anticonvulsants: A COG Study (Daily x5 every 3 weeks) 4- Saint Jude Children's Research Hospital: A Phase I Study of Irinotecan (CPT- 11) in Pediatric Patients with Refractory Solid Tumors (Daily x5, x2 every 3 weeks)

Phase II Studies:
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Tumor types: previously treated Ewing's sarcoma/ PNET, neuroblastoma, osteosarcoma, rhabdomyosarcoma, and other extracranial solid tumors; and medulloblastoma, glioma, ependymoma, brain stem glioma, and other CNS tumors

2- D9802: A Phase II "Up- Front Window Study" of Irinotecan (CPT- 11) Followed by Multimodal, Multiagent Therapy for Selected Children and Adolescents with Newly Diagnosed Stage 4/ Clinical Group IV Rhabdomyosarcoma: An IRS- V Study (Daily x 5, x 2 every 3 weeks)
Tumor type: previously untreated rhabdomyosarcoma

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the

investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # _35,229_ YES /_X_/ NO /___/ Explain: _____

Investigation #2

IND # _35,229_ YES /_X_/ NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_X_/

If yes, explain: _____

_____

Signature /S/ Date June 24, 2004
Title: Project Manager

/S/

Signature of Office/ Division Director Date See appended electronic signature in DFS

Form OGD-011347 Revised 05/10/2004

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Richard Pazdur
6/29/04 03:26:58 PM

MUST BE COMPLETED BY FILING DATE (60 DAYS)

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 20-571 **Supplement Type (e.g. SE5):** SE8 **Supplement Number:** 021

Stamp Date: December 24, 2003 **Action Date:** June 24, 2004

HFD-150 **Trade and generic names/dosage form:** Camptosar® (irinotecan hydrochloride)

Applicant: Pfizer Inc. **Therapeutic Class:** Cytotoxic 5010100

Indication(s) previously approved: Colorectal cancer

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 0 This supplement is not seeking an indication for Camptosar in pediatric patients. The Pharmacokinetcs in Special Populations – "Pediatric" and the "Pediatric Use" sections of the package insert based on the results of the studies are included in this submission.

Indication #1: The original application had a full waiver for colorectal cancer

Is there a full waiver for this indication (check one)?

☑ **Yes: Please proceed to Section A.**

☐ **No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed**
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☑ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:** _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**

- ☐ **Formulation needed**
- ☐ **Other:**_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

_____

Regulatory Project Manager

[redacted]

[redacted]

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Brenda Atkins
6/22/04 09:33:39 AM

Pediatric Exclusivity Board

March 10, 2004

Pediatric Exclusivity Board Members Representatives	Review Division/ Office
John Jenkins OND	Amna Ibrahim, HFD 150
Diane Murphy OPDD	William Rodriguez, Peds Team
Shirley Murphy, Director DPDD	Dragos Roman, HFD 510
Debbie Avant, Peds Team	Alan Shapiro, Peds Team
Robert Justice, HFD - 180	Solomon Iyasu, Peds Team
Badrul Chowdhury, HFD - 570	Liz Sadove
Sonal Vaid - OCC	Robert Justice
Dena Hixon, HFD 600	Louis Cooper, Peds Team
Edward Cox	Grace Carmouze, Peds Team
Sarah Goldkind	Roshni Ramchandani, OCPB
Aileen Ciampa	
Elizabeth Dickinson, OCC	
John Lazor	

Pediatric Exclusivity Determination for Camptosar (irinotecan) Injectable – Pfizer {NDA 20 - 571}

Initial Written Request:	January 22, 2001
Timeframe for submission of studies:	December 31, 2003
Date report of studies submitted:	December 22, 2003
Due Date for Pediatric Exclusivity Determination:	March 22, 2004

- The division noted that the sponsor submitted interim study reports from phase I and phase II trials rather than final reports to the agency.
- There was discussion regarding additional safety information resulting from the pediatric studies. The Board requested the division to consider putting safety information from the pediatric studies into the product label.
- The sponsor addressed each and every item in the Written Request satisfactorily.
- Division believes sponsor fairly met the terms of the Written Request.

Recommendations:

- Board agreed that the sponsor fairly met all terms in the Written Request.
- Pediatric Exclusivity granted
- Division was instructed to inform the sponsor via telephone that Pediatric Exclusivity was granted. The fact that exclusivity was granted will be posted on the pediatric web site and the exclusivity will be reflected in the next monthly update to the Orange Book.

/S/

Prepared by: _____ Date: _____
Debbie Avant, R.Ph.

/S/

_____ Date: _____
John Jenkins, M.D.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Debbie Avant
3/23/04 04:42:50 PM

sNDA #20-571

Drug Name Camptosar® Injection (irinotecan hydrochloride)

DEBARMENT CERTIFICATION

[FD&C Act 306(k)(1)]

Pfizer hereby certifies that it did not and will not use in any capacity the service of any person debarred under Section 306 of the Food, Drug and Cosmetic Act in connection with this application.

Signature of Company Representative

11/25/03

Date

Atkins, Brenda J

From: Ramchandani, Roshni
Sent: Thursday, June 24, 2004 10:53 AM
To: Atkins, Brenda J
Subject: FW: Camptosar

-----Original Message-----
From: Booth, Brian P
Sent: Monday, June 14, 2004 5:10 PM
To: Williams, Grant A; Dagher, Ramzi; Johnson, John R; Ibrahim, Amna
Cc: Mehta, Mehul U; Rahman, Nam Atiqur; Gobburu, Jogarao V; Ramchandani, Roshni
Subject: Camptosar

Good evening

We have essentially completed our review of Camptosar-pediatric supplement, and we want to run our recommendations by you.

1. Roshni did some PM work that indicated a trend in grade ¾ diarrhea and grade ¾ neutropenia for CPT-11 (SN-38 AUC) in adults and kids. Due to limitations in the PK data we would like to recommend the collection of PK samples (sparse sampling approach) in future studies of CPT-11 in adults or peds.

2. As SN-38 is glucoronidated and subsequently eliminated (partly) by UGT1A1, we would like to recommend that the sponsor report any UGT1A1 polymorphism data already collected, and to collect this information in future trials in adults or peds.

3. We would like to recommend that the PK information in peds be included in the labeling (probably a couple of sentences in the PK section, with a clear disclaimer about the lack of effectiveness). I realize that this proposal is contrary to our previous discussion, and I apologize for the about –face, but after reviewing the NDA and extensive discussion in the CPB briefing, we think that it is more consistent to include the data in the labeling. Our overall concern is that if the data is not included here, it will not be available to the oncology community. Conversely, we don't think the inclusion of the data will adversely affect the use of CPT-11.

Please let us know if you have any questions/comments.

Thanks

Brian

235 East 42nd Street
New York, NY 10017-5755

June 24, 2004

Dr. Richard Pazdur, Director
Division of Oncology Products (HFD-150)
Food and Drug Administration, CDER
Document Control Room 3rd Floor, Room 3067
Woodmont II Building
1451 Rockville Pike
Rockville, MD 20852

RE: Camptosar® (irinotecan HCl injection)
NDA 20-571
Labeling Supplement: Final

Dear Dr. Pazdur,

Reference is made to the December 2004 pediatric labeling submission (SN 021) for Camptosar®(irinotecan HCl injection), which was part of the Pediatric Written Request, granted by the FDA. Further reference is made to subsequent labeling negotiations on June 18, 22 and 23, 2004. Pfizer formally accepts the labeling proposal provided to us. Attached, please find the final agreed upon labeling for the product.

In accordance with the regulations, Pfizer intends to submit copies of the final printed labeling within 120 days of production.

If you have any questions, please call me at (212) 733-6565 or fax me at (212) 857-3558.

Sincerely,

Kristina D. Spranger
Sr. Manager, US Regulatory Affairs

cc: Brenda Atkins* – DODP Consumer Safety Officer

*cover letter via fax

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICATION INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Pharmacia & Upjohn	06/24/04
TELEPHONE NO. (*Include Area Code*)	FACSIMILE (FAX) Number (*Include Area Code*)
212-573-3412	212-857-3558
APPLICANT ADDRESS (*Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued*):	AUTHORIZED U.S. AGENT NAME & ADDRESS (*Number, Street, City, State, ZIP Code, telephone & FAX number*) IF APPLICABLE
235 East 42nd Street New York, NY 10017	Pfizer Inc 235 East 42nd Street New York, NY 10017

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (*If previously issued*) 20-571

ESTABLISHED NAME (*e.g., Proper name, USP/USAN name*)	PROPRIETARY NAME (*trade name*) IF ANY
Irinotecan Hydrochloride Injection	Camptosar® Injection

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (*If any*)	CODE NAME (*If any*)
(4S)-4,11-diethyl-4-hydroxy-9[(4-piperidinopiperidino) carbonyloxy]-1H-pyrano[3',4':6,7] indolizino {1,2-b}quinolone-3,14(4H,12H)dione Hydrochloride	CPT-11, PNY-101440E

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Injection	20 mg/mL	Intravenous

(PROPOSED) INDICATION(S) FOR USE: Component of first-line therapy in combination with 5-fluorouracil and leucovorin for patients with metastic carcinoma of the colon or rectum.

APPLICATION INFORMATION

APPLICATION TYPE
(check one) ☐ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug Holder of Approved Application

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☒ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION
Final clean & red-line package insert

PROPOSED MARKETING STATUS *(check one)* ☐ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED _____ THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

IND 35,229

This application contains the following items: (*Check all that apply*)	
	1. Index
	2. Labeling *(check one)* ☐ Draft Labeling ☒ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50 (d)(1); 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g., 21 CFR 314.50 (e)(2)(i); 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50 (d)(2); 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50 (d)(3); 21 CFR 601.2)
	7. Clinical Microbiology (e.g., 21 CFR 314.50 (d)(4))
	8. Clinical data section (e.g., 21 CFR 314.50 (d)(5); 21 CFR 601.2)
	9. Safety update report (e.g., 21 CFR 314.50 (d)(5)(vi)(b); 21 CFR 601.2)
	10. Statistical section (e.g., 21 CFR 314.50 (d)(6); 21 CFR 601.2)
	11. Case report tabulations (e.g., 21 CFR 314.50 (f)(1); 21 CFR 601.2)
	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C 355 (b)(2) or (j)(2)(A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.50 (l)(3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. Financial Information (21 CFR Part 54)
X	20. OTHER *(Specify) Final clean & red-line package insert*

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Brad Leglise for	Robert B. Clark Vice President US Regulatory	06/24/04

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
235 East 42nd Street New York, NY 10017	(212) 573-3412

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Dr., Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Pfizer, Inc.
235 E. 42nd Street
150/7/5
New York City, NY 10017

facsimile transmittal

To:	Brenda Atkins	Fax:	(301) 594-0498
From:	Kristina Spranger	Date:	6/24/2004
Re:	NDA 20-571 (Camptosar)	Pages:	3
CC:			

☐ Urgent ☐ For Review ☐ Please Comment ☐ Please Reply ☐ Please Recycle

Dear Ms. Atkins:

Please find enclosed a faxed copy of Pfizer's acceptance of the final pediatric labeling (June 23, 2004).

Attached, please find the cover letter and 356h for our submission, which will include the final agreed-upon labeling.

Kind Regards,

Kristina Spranger

6/24/04

PROJECT MANAGER REVIEW OF LABELING

NDA 20-571/SE8-021

Drug: Camptosar® Injection **Tradename: irinotecan hyrdrochloride injection**

Applicant: Pfizer Inc.

Submission Date(s):	**Receipt Date(s):**
December 22, 2003	December 24, 2003
January 21, 2004	January 22, 2004
May 16, 2002	May 20, 2002
June 7, 2002	June 10, 2002

BACKGROUND:

The submission, NDA 20-571/S021 was submitted to the Electronic Document Room in response to the Agency's January 22, 2001 Written Request letter and filed as: \\CDSESUB1\N20571\S 021\2003-12-22 and \\CDSESUB1\N20571\S_021\2004-01-21 and consist of proposed labeling changes in the applicant's package insert identified as "Draft November 2003", with copy code 816 907 113 based upon pediatric study reports. Pediatric Exclusivity was granted on March 11, 2004.

DOCUMENTS REVIEWED:

May 16, 2002	Pfizer	Final Printed Labeling (FPL) in response to approval of S-016
June 7, 2002	Pfizer	Final Printed Labeling in response to approval of S-016 (sponsor correction of May 16, 2002 FPL)
December 22, 2003	Pfizer	Proposed Pediatric Labeling submitted December 22, 2003 in Adobe Acrobat format
January 21, 2004	Pfizer	Proposed Pediatric Labeling submitted January 21, 2004 in Word format as minor abeling amendment (BL)

An FA was submitted on May 16, 2002 and a correction to it on June 7, 2002 in response to supplement 016; however, no action was ever taken on the two FA submissions. They both should be acknowledged and retained. The applicant's FPL submitted on June 7, 2002 and May 16, 2002 were compared with the labeling attached to the Agency's May 16, 2002 approval letter of S-016 and no differences were found other than editorial and punctuation.

REVIEW:

The sponsor's proposed revised wording was under the **CLINICAL PHARMACOLOGY**, **Pharmacokinetics in Special Populations,** *Pediatric* section of the package insert identified as "Draft November 2003", which is copied below:

[

]

On June 18, 2004 the Agency proposed that all of the above should be deleted from the *Pediatric* section and replaced with the following:

Pediatric: See **Pediatric Use** in the **PRECAUTIONS** section.

Pfizer's additional proposed changes were made under the PRECAUTIONS, Pediatric Use subsection and were as follow:

The Agency's June 18, 2004, proposed revisions were the following:

Pediatric Use

~~The safety and effectiveness of CAMPOTSAR in pediatric patients have not been established.~~

The effectiveness of irinotecan in pediatric patients has not been established. Results from two open-label, single arm studies were evaluated. One hundred and seventy children with refractory solid tumors were enrolled in one phase 2 trial in which 50 mg/m^2/day of irinotecan was infused for 5 consecutive days every 3 weeks. Grade 3- 4 neutropenia was experienced by 54 (31.8%) patients. Neutropenia was complicated by fever in 15 (8.8%) patients. Grade 3- 4 diarrhea was observed in 35 (20.6%) patients. [redacted] The adverse event profile was [redacted] that observed in adults. [redacted]

The applicant submitted on June 23, 2004 proposed labeling revisions dated June 22, 2004 to the Pediatric use subsection in response to the Agency's June 18, 2004 proposed labeling revisions (see below).

Pediatric Use

~~The safety and effectiveness of CAMPOTSAR in pediatric patients have not been established.~~

The effectiveness of irinotecan in pediatric patients has not been established. Results from two open-label, single arm studies were evaluated. One hundred and seventy children with refractory solid tumors were enrolled in one phase 2 trial in which 50 mg/m^2 of irinotecan was infused for 5 consecutive days every 3 weeks. Grade 3- 4 neutropenia was experienced by 54 (31.8%) patients. Neutropenia was complicated by fever in 15 (8.8%) patients. Grade 3- 4 diarrhea was observed in 35 (20.6%) patients. This adverse event profile was comparable to that observed in adults. In the second phase 2 trial of 21 children with previously untreated rhabdomyosarcoma, 20 mg/m^2 of irinotecan was infused for 5 consecutive days on weeks 0, 1, 3 and 4. This single agent therapy was followed by multimodal therapy. Accrual to the single agent irinotecan phase was halted due to the high rate (28.6%) of progressive disease and the early deaths (14%) [redacted] The adverse event profile was different in this study

from that observed in adults; the most significant grade 3 or 4 adverse events were dehydration experienced by 6 patients (28.6%) associated with severe hypokalaemia in 5 patients (23.8%) and hyponatremia in 3 patients (14.3%); in addition Grade 3-4 infection was reported in 5 patients (23.8%)(across all courses of therapy and irrespective of causal relationship).
Pharmacokinetic parameters for irinotecan and SN-38 were determined in 2 pediatric solid-tumor trials at dose levels of 50 mg/m^2 (60-min infusion, n=48) and 125 mg/m^2 (90-min infusion, n=6). Irinotecan clearance (mean ± S.D.) was 17.3 ± 6.7 L/h/m^2 for the 50 mg/m^2 dose and 16.2 ± 4.6 L/h/m^2 for the 125 mg/m^2 dose, which is comparable to that in adults. Dose-normalized SN-38 AUC values were comparable between adults and children. Minimal accumulation of irinotecan and SN-38 was observed in children on daily dosing regimens [daily x 5 every 3 weeks or (daily x 5) x 2 weeks every 3 weeks].

The Agency agreed with the applicant's proposed wording with the exception of the following sentence:

"Accrual to the single agent irinotecan phase was halted due to the high rate (28.6%) of progressive disease and the early deaths (14%) [ ]

We communicated to the sponsor on June 23, 2004 that [ ] should be deleted and the sentence should read as follows.

"Accrual to the single agent irinotecan phase was halted due to the high rate (28.6%) of progressive disease and the early deaths (14%). [ ]

Lastly, it was noted that the REFERENCES section of the November 2003 package insert was missing 1 of 8 references and the sponsor was advised to insert the following:

1. ONS Clinical Practice Committee. Cancer Chemotherapy Guidelines and Recommendations for Practice Pittsburgh, Pa: Oncology Nursing Society; 1999:32-41.

The applicant accepted the insertion of the above reference in the REFERENCES section on June 23, 2004 and officially by letter dated June 24, 2004.

CONCLUSION - RECOMMENDED REGULATORY ACTION:

The PI submitted to the sponsor on June 23, 2004 was agreed upon by both the applicant and the Agency and will be attached to the Action Letter for S-021. I compared the FA word document submitted to EDR dated June 7, 2002 with the June 23, 2004 labeling and there were only minor editorial changes and no major wording changes. With concurrence of the reviewers, this supplement may be approved and the FA acknowledged and retained.

/s/ June 23, 2004 /s/ June 24, 2004

Brenda J. Atkins/Date
Regulatory Project Manager

Dotti Pease
CPMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Brenda Atkins
6/24/04 02:21:54 PM
CSO

Dotti Pease
6/24/04 02:32:12 PM
CSO

Regulatory Affairs
Pfizer Inc
235 East 42nd Street 150/7/5
New York, NY 10017
Tel 212 573 2620 Fax 212 857 3558
Email melinda.rudnicki@pfizer.com

Pfizer Pharmaceuticals Group

June 9, 2004

Melinda Rudnicki
Director
Worldwide Regulatory Strategy

Richard Pazdur, M.D., Director
Division of Oncology Drug Products, HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 3rd Floor
Woodmont II Building
1451 Rockville Pike
Rockville, MD 20852

RE: Camptosar (irinotecan HCl injection)
NDA # 20-571
Safety Update Report

Dear Dr. Pazdur:

Reference is made to Pfizer's NDA # 20-571 for Camptosar (irinotecan HCl injection) and the December 22, 2003 submission of pediatric Study Reports. This submission contains a Safety Update for the above referenced product covering the period from September 1, 2003 to March 31, 2004. All safety information reported to Legacy Pharmacia of serious adverse events records of patients 22 years of age or younger treated with Camptosar where reviewed.

In summary, no safety data were found which would adversely affect the safety conclusions supported in our December 22, 2003 Camptosar pediatric submission. Please include this information in our file for Camptosar, NDA # 20-571. Should you require any additional information, please feel free to contact me at 212-573-2620.

Sincerely,

Melinda Rudnicki

Cover letter:
Brenda J. Atkins, Regulatory Project Manager
Division of Oncology Drug Products, HFD-150
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 3rd Floor
Woodmont II Building
1451 Rockville Pike
Rockville, MD 20852

5/10/04

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

NDA 20-571

Pfizer Inc.
Attention: Kristina Spranger
Senior Manager, US Regulatory Affairs
235 E. 42nd Street 150/7/5
New York City, NY 10017

Dear Ms. Spranger:

Please refer to the Written Request, originally issued on January 22, 2001, that you received from the Center for Drug Evaluation and Research, as well as the amendment issued in July 2002, from the Office of Counter-Terrorism and Pediatric Drug Development.

BPCA § 18: Minority Children and Pediatric Exclusivity Program

We are amending the "Format of reports to be submitted" section of your Written Request to require submitted reports to include more specific information on racial and ethnic minorities, in accordance with Section 18, *Minority Children and Pediatric-Exclusivity Program*, of the Best Pharmaceuticals for Children Act (BPCA) (Public Law 107-109). All other terms stated in our original Written Request remain the same.

> *Format of reports to be submitted:*
> In addition, the reports are to include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the study(s) must be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander or White. For ethnicity one of the following designations must be used: Hispanic/Latino or Not Hispanic/Latino.

BPCA § 9: Public Dissemination of Medical and Clinical Pharmacology Review Summaries for All Fileable Supplements Submitted in Response to Written Requests

We note that the July 2002 re-issued Written Request notified you that an application submitted in response to a Written Request would be subject to the disclosure provisions of the BPCA. This letter also reminds you that in accordance with Section 9 of the BPCA, *Dissemination of Pediatric Information*, if a pediatric supplement is submitted in response to a Written Request and filed by FDA, FDA will make public a summary of the medical and clinical pharmacology reviews of pediatric studies conducted. This disclosure, which will occur within 180 days of supplement submission, will apply to all supplements submitted in response to a Written Request issued or re-issued under BPCA and filed by FDA, regardless of the following circumstances:

(1) the type of response to the Written Request (complete or partial);
(2) the status of the supplement (withdrawn after the supplement has been filed or pending);
(3) the action taken (i.e. approval, approvable, not approvable); or
(4) the exclusivity determination (i.e. granted or denied).

FDA will post the medical and clinical pharmacology review summaries on the FDA website at [http://www.fda.gov/cder/pediatric/Summaryreview.htm] and publish in the Federal Register a notification of availability.

If you have questions regarding the BPCA, please contact the Division of Pediatric Drug Development at (301) 594-7337. As noted above, requests to amend your Written Request should be directed to the review division.

Sincerely,

{See appended electronic signature page}

M. Dianne Murphy, M.D.
Director
Office of Counter-terrorism and Pediatric Drug Development
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Dianne Murphy
5/10/04 08:32:18 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 03 March 2004

TO: Melinda Rudnicki
Phone (212) 733-2620
Fax (212) 857-3558

FROM: Brenda J. Atkins, Regulatory Project Manager

NDA/DRUG: 20-571/S-021 - Camptosar® Injection (Irinotecan Hydrochloride Injection)

SUBJECT: Supplemental NDA for Pediatric Exclusivity - Clinical Pharmacology and Biopharmaceutics Reviewer Request

Please refer to your submission dated December 22, 2003.

Please send the raw safety data sets along with subject demographics and dosage information for the following Phase 1 and phase 2 trials:

Phase 1 studies
Protocol # 98-6475-178
Protocol # M6475056
Protocol #:CPTAIV-0020-452
Protocol # CPTAIV-0020-453

Phase 2 studies
Protocol # 440E-ONC-0020-222
Protocol # 440E-ONC-0020-207

The files should be sent in SAS transport format (*.xpt).

Please call me at 301-594-5767 if there are any questions.

Thanks.

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/s/

Brenda Atkins
3/3/04 01:08:06 PM
CSO

From: Rudnicki, Melinda [melinda.rudnicki@pfizer.com]
Sent: Tuesday, March 16, 2004 11:55 AM
To: 'Atkins, Brenda J'
Subject: RE: Camptosar: NDA 20-571/S-021
Thanks for the good news.

Melinda
-----Original Message-----
From: Atkins, Brenda J [mailto:ATKINSB@cder.fda.gov]
Sent: Tuesday, March 16, 2004 9:08 AM
To: 'melinda.rudnicki@pfizer.com'
Subject: Camptosar: NDA 20-571/S-021

Dear Melinda:

On March 11, 2004, the Pediatric Exclusivity Board (PEB) determined that they would grant pediatric exclusivity to Camptosar. This will appear in the Orange Book soon (I believe within 3-4 weeks).

The PEB also instructed me to the convey the following:

Section 5 of the BPCA outlines the dispute resolution process when the sponsor and Agency fail to come to an agreement on labeling. Any labeling dispute must be resolved by an Advisory Committee within 180 days.

In addition, the pediatric studies will be posted on the internet within 180 days of your submission. Pfizer will receive no other notification re. the granting of pediatric exclusivity.

In the meantime, our review of S-021 continues with an action date of 6-24-04.

Sincerely,

Brenda Atkins, Regulatory Project Manager
Division of Oncology Drug Products
Center for Drug Evaluation and Research
Phone: (301) 594-5767/Fax: (301) 594-0498

"MMS <secure.pfizer.com>" made the following
annotations on 03/16/2004 09:08:37 AM

This message was sent in secure form from cder.fda.gov CDER Stamp

==========

"MMS <secure.pfizer.com>" made the following
annotations on 03/16/2004 11:54:55 AM

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/s/

Brenda Atkins
6/22/04 11:16:04 AM
CSO

Atkins, Brenda J

From: Avant, Debbie
Sent: Thursday, March 11, 2004 10:06 AM
To: Atkins, Brenda J
Cc: Carmouze, Grace N; Ibrahim, Amna
Subject: PE Granted for Irinotecan

Brenda,

Pediatric Exclusivity was granted for Irinotecan. Please in form the Sponsor that Pediatric Exclusivity was granted and will appear in the Orange Book soon. Section 5 of BPCA outlines the dispute resolution process when the Sponsor and the Agency fail to come to an agreement on labeling. Any labeling dispute must be resolved by the Advisory Committee within 180 days. In addition, advise the Sponsor that the pediatric studies will be posted on the internet within 180 days of their submission.

Thanks,

Debbie

3/10/04

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST

PART I - TO BE COMPLETED BY THE REVIEWING DIVISION.

Date of Written Request from FDA 01/22/2001 Application Written Request was made to: NDA/IND# NDA 20-571
Timeframe Noted in Written Request for Submission of Studies 12/31/03.
NDA# 20-571 Supplement # 021 Choose one: SE1 SE2 SE3 SE4 SE5 SE6 SE7 **SE8** SLR
Sponsor Pfizer Inc.
Generic Name irinotecan HCL Trade Name Camptosar®
Strength 20mg/mL Dosage Form/Route injection/intravenous
Date of Submission of Reports of Studies 12/22/03.
Pediatric Exclusivity Determination Due Date (60 or 90 days from date of submission of studies) 03/22/04.

Was a formal Written Request made for the pediatric studies submitted?	Y √	N ___
Were the studies submitted after the Written Request?	Y √	N ___
Were the reports submitted as a supplement, amendment to an NDA, or NDA?	Y √	N ___
Was the timeframe noted in the Written Request for submission of studies met?	Y √	N ___
If there was a written agreement, were the studies conducted according to the written agreement? OR If there was no written agreement, were the studies conducted in accord with good scientific principles?	Y √	N ___
Did the studies fairly respond to the Written Request?	Y √	N ___

SIGNED /S/ DATE 3/10/04
(Reviewing Medical Officer)

Do not enter in DFS - FORWARD TO PEDIATRIC EXCLUSIVITY BOARD, HFD-960.

PART II - TO BE COMPLETED BY THE PEDIATRIC EXCLUSIVITY BOARD

Pediatric Exclusivity ✓ **Granted** ___ **Denied**

Existing Patent or Exclusivity Protection:

NDA/Product #	Eligible Patents/Exclusivity	Current Expiration Date
20-571	4604463	AUG 20, 2007
20-571	6403569	APR 28, 2020

SIGNED /S/ DATE 3/10/04

Revised: 11/30/2001

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/s/

Debbie Avant
3/11/04 11:55:14 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS
Pfizer Inc. acting as agent for Pharmacia & Upjohn
235 East 42nd Street
New York, NY 10017

2. TELEPHONE NUMBER *(Include Area Code)*
(212) 573-3414

3. PRODUCT NAME
Camptosar (irinotecan HCl)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER
NDA # 20-571

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☐ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER
4659

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See Item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See Item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FORTHIS APPLICATION?
☐ YES ☒ NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
M Clark for R. Clark	Vice President US Regulatory	12/22/2003

FORM FDA 3397 (1/03)

PSC Media Arts (301) 443-1090 EF

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

DATE: 30 September 2003

TO: Christiane H. Vanderlinden, M.S., R.Ph.
Regulatory Affairs Manager
Phone (908) 901-6736
Fax (908) 901-6567

FROM: Brenda J. Atkins, Regulatory Project Manager

NDA/DRUG: 20-571 - Camptosar® Injection (Irinotecan Hydrochloride Injection)

SUBJECT: **FDA Comments re. Proposed sNDA for Pediatric Exclusivity**

Please refer to your submission dated August 21, 2003, received August 22, 2003, requesting FDA comments on a proposed sNDA for Pediatric Exclusivity. On page 23 of this submission, section 7 listed "**ISSUES FOR CONCURRENCE WITH FDA**". Your issues and our responses (**bolded**) to those issues are listed below.

You requested that the FDA provide agreement in response to the following:

1. Please refer to a discussion with Dr. Hirschfeld on September 12, 2002, and his request to document changes to our original PPSR submitted on October 30, 2000. Our July 1, 2003 submission outlines several minor changes to our October 2000 PPSR. Also submitted, on July 16, 2003, were several additional issues on the format of the submission. Please let us know if you have any issues with these clarifications.

FDA:

We have already replied to your July 16th, 2003 submission. Please refer to our August 25, 2003 telephone conversation in which you were told that your proposal regarding format of the sNDA was acceptable.

Regarding the July 1, 2003 submission, the amendments may be acceptable. We may require you to obtain and submit laboratory data from hospital or office records, depending on the amount of information received from the St. Jude Phase I study. Compliance with the Written Request will be a review issue.

2. CSF samples were not collected in any of the pediatric trials, which had the objectives of defining the safety profile, MTD, and plasma PK (Phase Is) or assessing efficacy and plasma PK (Phase IIs) rather than quantitating the CNS penetration of the drug. In addition multiple samples of CSF from each patient would be required to accurately define CNS penetration and this would be prohibitive in patients who did not have an indwelling reservoir. A further consideration in this regard is that the blood-brain barrier is believed to be disrupted in the vicinity of malignant brain tumors, allowing better drug penetration than might be predicted by measurements of the time-course of CSF drug levels. Does the FDA agree that collecting CSF in pediatric patients was not acceptable in these studies?

FDA: Yes.

3. Because treatment regimens and multiple tumor types were evaluated across the 6 trials, Pharmacia proposes that the safety data will be summarized separately by protocol and in parallel, tabular comparisons. Is this acceptable to the FDA?

FDA: This proposal appears acceptable.

4. Pharmacia proposes to revise the Clinical Pharmacology and Pediatric Use (Precautions) sections of the CAMPTOSAR™ package insert. These changes will summarize the safety and PK information derived from the 2 Phase II pediatric trials. Is this acceptable to the Agency?

FDA:

The changes made to the label will be a review issue. Your proposal appears acceptable.

Please call me at 301-594-5767 if there are any questions.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Brenda Atkins
9/30/03 03:16:27 PM
CSO

9/25/03

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 20-571	Efficacy Supplement Pediatric Exclusivity Labeling Supplement SE-8	Supplement Number 021	
Drug: CAMPTOSAR® (irinotecan hydrochloride)			
RPM: Brenda Atkins		HFD-150	Phone # 301-594-5767
Application Type: (√) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name): N/A	

❖ Application Classifications:	
• Review priority	( ) Standard (√) Priority
• Chem class (NDAs only)	N/A
• Other (e.g., orphan, OTC)	N/A
❖ User Fee Goal Dates	24 Jun 04
❖ Special programs (indicate all that apply)	(√) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review ( ) CMA Pilot 1 ( ) CMA Pilot 2
❖ User Fee Information	
• User Fee	(√) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (√) No
• This application is on the AIP	( ) Yes (√) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	(√) Verified
❖ Patent	
• Information: Verify that form FDA-3542a was submitted.	(√) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted.	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	(N/A) Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	X
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!*	( ) Yes, Application #_____ **(X)** No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	N/A
❖ Actions	
• Proposed action	(√) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only) N/A	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (√) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(√) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	X
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	11-19-03
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	N/A
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	N/A
• Reviews	N/A
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	N/A
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	X

❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
Medical Officer Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	N/A
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	June 14, 2004
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	June 9, 2004
❖ Risk Management Plan review(s) *(indicate date/location if incorporated in another rev)*	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	X
❖ Demographic Worksheet *(NME approvals only)*	N/A
❖ Statistical review(s) *(indicate date for each review)*	N/A
❖ Biopharmaceutical review(s) *(indicate date for each review)*	June 18, 2004
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	N/A
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	N/A
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Microbiology (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report) N/A	Date completed: ( ) Acceptable ( ) Withhold recommendation
❖ Methods validation N/A	( ) Completed ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	N/A
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

7/2/02

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

NDA 20-571

Pharmacia & Upjohn
Attention: Christiane H. Vanderlinden
Regulatory Affaris Manager
7000 Portage Road
Kalamazoo, MI 49001-0199

Dear Ms. Vanderlinden:

Please refer to the Written Request, originally issued on January 22, 2001, that you received from the Center for Drug Evaluation and Research. This Written Request was issued under Section 505A of the Federal Food, Drug, and Cosmetic Act to conduct pediatric studies using irinotecan hydrochloride. As you know, on January 4, 2002, the President signed into law the "Best Pharmaceuticals for Children Act," (BPCA) which both extended the pediatric exclusivity program established in the 1997 FDA Modernization Act (FDAMA) and provided new mechanisms for studying pediatric uses for drugs. The BPCA also contains new provisions of which you should be aware related to user fees, priority review, drug labeling, and disclosure of pediatric study results. FDA is revising its Guidance for Industry: Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act to provide additional information on the pediatric drugs study provisions of the BPCA.

FDA has received questions about whether sponsors who were issued Written Requests to conduct pediatric studies prior to passage of the BPCA, but who had not as yet submitted the reports of the studies as of January 4, 2002, would be governed by the provisions of FDAMA or the BPCA. In order to maximize the benefit to be derived from the BPCA and to minimize uncertainty and delay in implementing the pediatric exclusivity program, FDA has decided to reissue those Written Requests originally issued prior to passage of the BPCA for which studies have not already been submitted.

This letter is your notification that the Written Request (and any subsequent amendments) described above is considered to be reissued as of the date of this letter. The terms of the Written Request are not otherwise altered by this letter. If you believe that the Written Request should be amended, please contact the division directly.

Please note that if the original Written Request was issued under Section 505A(a), it will now be considered to be issued under Section 505A(b), due to the reordering of the sections, as described in Section 19 of the BPCA. If the original Written Request was issued under Section 505A(c), it will still be considered to be issued under Section 505A(c).

An important change to note is that, if the drug for which FDA issued the Written Request under 505A(c) has listed patent or exclusivity protection, new section 505(d)(4)(A) states that within 180 days of receipt of this "reissued" Written Request, you must notify FDA when the pediatric studies will be initiated, or that you do not agree to conduct the requested studies. New provisions at Section 505(d)(4)(B)-(F) describe alternative methods for obtaining these pediatric studies.

If you have questions regarding the BPCA, please contact the Division of Pediatric Drug Development at (301) 594-7337. As noted above, requests to amend your Written Request should be directed to the review division.

Sincerely,

{See appended electronic signature page}

M. Dianne Murphy, M.D.
Director
Office of Counter-terrorism and Pediatric Drug Development
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Dianne Murphy
7/2/02 08:52:51 PM

1/22/01

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Division of Oncology Drug Products
Food and Drug Administration
Rockville MD 20857

NDA 20-571

Pharmacia & Upjohn
Attention: Christiane H. Vanderlinden
Regulatory Affairs Manager
7000 Portage Road
Kalamazoo, MI 49001-0199

Dear Ms. Vanderlinden:

Reference is made to your Proposed Pediatric Study Request submitted on October 30, 2000 for CAMPTOSAR® Injection (irinotecan hydrochloride) to NDA 20-571.

To obtain needed pediatric information on CAMPTOSAR® Injection (irinotecan hydrochloride) the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), that you submit specific pediatric studies, detailed later in the letter. These studies investigate the potential use of CAMPTOSAR® Injection (irinotecan hyrdochloride) in the treatment of children with solid tumors.

The development of pediatric oncology drugs merits special consideration. Compared to adult malignancies, pediatric cancers afflict small numbers of patients. Because the majority of pediatric patients receive their cancer therapy as participants in clinical research protocols, participation in Phase 3 oncology trials has become the *standard of care* in pediatric oncology. Children with cancer are usually treated at specialized centers by pediatric oncologists who are members of a national pediatric cooperative study group. One of the highest priorities of these groups is to develop improved novel therapies. Early access to new drugs is one mechanism to achieve this goal.

Known and potential differences in the biology of pediatric and adult tumors will often preclude the extrapolation of clinical activity from adults to children. Therefore, it is usually impossible to rely on pharmacokinetic and safety data alone to guide the use of these drugs in children. It is imperative that we evaluate the effectiveness and safety of new drugs in pediatric populations. In most cases, in the absence of available therapies to treat refractory stages of most pediatric cancers, the FDA expects to be able to use flexible regulatory approaches in developing and approving drugs for pediatric tumors (e.g., basing approval on an effect on tumor size or other surrogate marker likely to predict clinical benefit (Subpart H), and/or based on safety in smaller numbers of patients (Subpart E).

The intent of designing studies for development of drugs for pediatric oncology is to proceed in the context of an overall development program. Drugs that lack dosing and pharmacokinetic information should begin with Phase 1 studies. Drugs that have dosing and pharmacokinetic data in pediatric patients should be tested in Phase 2 or pilot studies. If appropriate, a specific disease may be targeted; otherwise, several studies in a variety of tumor types, such as brain tumors, solid tumors, or hematologic tumors should be planned. Depending upon the outcome of the Phase 2 studies, Phase 3 studies may be initiated. Please refer to the **Guidance for Industry Pediatric Oncology Studies In Response to a Written Request** located on the web at www.fda.gov/cder/guidance/3756dft.htm for circumstances when it may be appropriate to request an exclusivity determination or advisory opinion at the end of either Phase 1 or 2.

Protocols for each of your studies should be submitted to the FDA for review, but they need not be submitted simultaneously. For example, if you begin with a Phase 1 study, initially a Phase 1 protocol should be submitted for review, but the submission of Phase 2 or pilot study protocols may be deferred.

REQUESTED STUDIES:

Please submit information from the following types of studies:

- ***Type of studies:***

  Phase 1: A dose finding study including pharmacokinetics, with doses determined for all appropriate age groups and schedules of treatment. The number of patients entered should be sufficient to achieve Phase 1 objectives, which may be in the range of 18-25.

  Phase 2 or pilot studies: Enrollment of at least 14 pediatric patients per trial, in refractory or relapsed tumors. Studies should be performed at facilities that have the experience, support, and expertise to care for children with cancer.

- ***Indication(s) to be studied (i.e., objective of each study):***

  (1) Refractory or relapsed pediatric solid tumors (metastatic rhabdomyosarcoma, Ewing's sarcoma, neuroblastoma, osteosarcoma, medulloblastoma, brain stem glioma and ependymoma)

  (2) Previously untreated metastatic rhabdomyosarcoma

- ***Age group in which study(ies) will be performed:***

  Infants > 1 month of age to adolescents

- ***Study endpoints:***

  The pharmacokinetic study will have maximum tolerated dose (MTD) (or biologically effective dose = BED) as a primary endpoint with measurements of blood (and CSF if appropriate) concentrations, clearance, and distribution in body compartments as secondary endpoints. The Phase 2 studies or pilot studies should have a disease-specific surrogate or clinically relevant endpoint.

- ***Drug information:***

  Dosage form: Intravenous
  Route of administration: Intravenous
  Regimen: As determined by Phase 1/2 studies

- ***Drug specific safety concerns:*** diarrhea, myelosuppression and potential pharmacokinetic interaction with anticonvulsants

- ***Statistical information, including power of study and statistical assessments:***

  Descriptive statistics

- ***Labeling that may result from the study(ies):***

  Appropriate sections of the label may be changed to incorporate the findings of the studies.

- ***Format of reports to be submitted:***

  Full study reports not previously submitted to the Agency addressing the issues outlined in this request with full analysis, assessment, and interpretation.

- ***Timeframe for submitting reports of the study(ies):***

  Reports of the above studies must be submitted to the Agency on or before December 31, 2003. Please keep in mind that pediatric exclusivity attaches to existing patent protection or exclusivity that has not expired or been previously extended at the time you submit your reports of the studies in response to this Written Request.

Please submit protocols for the appropriate studies to your investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission.

Reports on the outcome of the studies should be submitted to a new drug application (NDA) or a supplement to an approved NDA with the proposed labeling you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if changes to this Written Request are agreed to by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you to develop additional pediatric information that may produce health benefits in the pediatric population. If you have any questions, call Brenda Atkins at 301-594-5767.

Sincerely yours,

/S/

Rachael E. Behrman, MD, MPH
Deputy Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

/s/

Rachel Behrman
1/22/01 10:02:10 AM

Atkins, Brenda J

From: Atkins, Brenda J
Sent: Thursday, June 24, 2004 4:05 PM
To: CDER-APPROVALS; CDER-OND-150-GROUP; Quinn, Kathleen K.; Grillo, Joseph
Subject: Approval of NDA 20-571/S-021

Today, the Division of Oncology Drug Products approved the following supplement:

NDA:	20-571/S-021 (**The applicant obtained pediatric exclusivity)**
Drug:	Camptosar (irinotecan hydrochloride)
Applicant:	Pfizer Inc
Approval Date:	June 24, 2004
Original Indication:	Camptosar is indicated as a component of first-line therapy in combination with 5-fluorouracil and leucovorin for patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following initial fluorouracil-based therapy
Route of administration:	I.V.
Rx or OTC:	Rx

The approval letter and labeling are attached.

090014648043a3d2
.pdf (208 KB)

Atkins, Brenda J

From: Atkins, Brenda J
Sent: Wednesday, June 23, 2004 11:14 AM
To: 'Kristina.Spranger@Pfizer.com'
Subject: Proposed labeling revisions re. Camptosar

Importance: High

Dear Kristina:

Attached are the Agency's proposed labeling revisions in reference to your 12-22-03 sNDA for Pediatric Exclusivity and in response to your June 22, 2004 proposed labeling revisions. The Agency concurs with all of your revisions with the exception of page 19, Pediatric Use (see PI attached) subsection.

The following is our proposed change:

Accrual to the single agent irinotecan phase was halted due to the high rate (28.6%) of progressive disease and the early deaths (14%).

The sentence above should read as follows:

"Accrual to the singe agent irinotecan phase was halted due to the high rate (28.6%) of progressive disease and the early deaths (14%)."

The PI with your and our revisions are attached. A clean copy is also attached.

Please review and make a determination to accept or make additional revisions. If you accept our revisions please submit your acceptance via fax with an official submission to your NDA. The Action Date is June 24, 2004.

Thanks--Brenda Atkins, Project Manager


S-021 2nd draft for industry n...


S-021 2nd draft for industry n...

34 pages redacted from this section of the approval package consisted of draft labeling

Atkins, Brenda J

From: Ibrahim, Amna
Sent: Wednesday, June 23, 2004 10:30 AM
To: Atkins, Brenda J
Subject: FW: Camptosar Pediatric Labeling - S-021 2nd draft for FDA negotiatio n 6-22-04

Brenda
As discussed, the line should read as
Accrual to the single agent irinotecan phase was halted due to the high rate (28.6%) of progressive disease and the early deaths (14%)
The struck out portion should be deleted. Pharmacia's changes on page 19 are otherwise OK
Amna

----Original Message-----
From: Johnson, John R
Sent: Wednesday, June 23, 2004 10:26 AM
To: Ibrahim, Amna
Subject: RE: Camptosar Pediatric Labeling - S-021 2nd draft for FDA negotiatio n 6-22-04

As discussed.

John

-----Original Message-----
From: Ibrahim, Amna
Sent: Wednesday, June 23, 2004 10:13 AM
To: Johnson, John R
Subject: FW: Camptosar Pediatric Labeling - S-021 2nd draft for FDA negotiatio n 6-22-04
Importance: High

Dr Johnson,
Action Date for this supplement is tomorrow.

Pharmacia wants to add the portions highlighted in yellow.

I am fine with their suggestion except I do not want to put any particular cause to the reason of death. I would preefr to leave the sentence as before:

I will leave a paper copy on your chair. Additionally, the whole label is attached.

Amna

-----Original Message-----
From: Atkins, Brenda J
Sent: Tuesday, June 22, 2004 4:58 PM
To: Ramchandani, Roshni; Ibrahim, Amna
Subject: FW: Camptosar Pediatric Labeling - S-021 2nd draft for FDA negotiatio n 6-22-04
Importance: High

Roshni and Amna:

Please look over Pfizer's counter proposal to our changes. Let me know soon whether you agree or disagree.

Thanks--Brenda
-----Original Message-----
From: Spranger, Kristina [mailto:Kristina.Spranger@pfizer.com]
Sent: Tuesday, June 22, 2004 4:49 PM
To: 'ATKINSB@cder.fda.gov '
Cc: PPG FIO Mailbox; Spranger, Kristina
Subject: Camptosar Pediatric Labeling - S-021 2nd draft for FDA negotiatio n 6-22-04

Dear Brenda -
Please refer to our NDA 20-571 for Camptosar.

Attached, please find Pfizer's proposed labeling changes based upon the FDA's proposal sent to us on Friday, June 18. Our insertions are highlighted in yellow and deletions in blue strikethrough notations.

We are including information which we hope will assist patients and physicians in better understanding the data available with regard to the pediatric population.

We look forward to receiving your response. Please be aware that I am off-site, so it would be much appreciated if you could email me the next proposal (if necessary) or contact me via cellular telephone (917)763-0372.

Kind Regards,
Kristina Spranger
Sr. Manager
US Regulatory
Pfizer Inc.

"MMS <secure.pfizer.com>" made the following
annotations on 06/22/2004 04:49:04 PM
---

2 pages redacted from this section of the approval package consisted of draft labeling

Atkins, Brenda J

From: Spranger, Kristina [Kristina.Spranger@pfizer.com]
Sent: Tuesday, June 22, 2004 4:49 PM
To: 'ATKINSB@cder.fda.gov '
Cc: PPG FIO Mailbox; Spranger, Kristina
Subject: Camptosar Pediatric Labeling - S-021 2nd draft for FDA negotiatio n 6-22-04


S-021 2nd draft for FDA negoti... mmsinfo.txt (459 B)

Dear Brenda -
Please refer to our NDA 20-571 for Camptosar.

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We look forward to receiving your response. Please be aware that I am off-site, so it would be much appreciated if you could email me the next proposal (if necessary) or contact me via cellular telephone (917)763-0372.

Kind Regards,
Kristina Spranger
Sr. Manager
US Regulatory
Pfizer Inc.

"MMS <secure.pfizer.com>" made the following
annotations on 06/22/2004 04:49:04 PM

Legal Notice

36 pages redacted from this section of the approval package consisted of draft labeling

Atkins, Brenda J

From: Booth, Brian P
Sent: Thursday, June 17, 2004 3:37 PM
To: Ibrahim, Amna; Atkins, Brenda J; Johnson, John R; Dagher, Ramzi; Ramchandani, Roshni
Subject: RE: Camptosar label

Yep.

-----Original Message-----
From: Ibrahim, Amna
Sent: Thursday, June 17, 2004 2:20 PM
To: Atkins, Brenda J; Johnson, John R; Dagher, Ramzi; Booth, Brian P; Ramchandani, Roshni
Subject: Camptosar label

<< File: Camp label-061704.doc >>
After addition of further toxicity data in the window study, I am sending this label around once more on . All changes are on page 19.

I have taken the liberty to delete what was put in by the sponsor in the PK section page 4, because it makes sense to have all pediatric info in one section. I believe Clin Pharm were not going to have any changes from this morning, so that section has also been put in the "Pediatric Use". Hope that's OK with the Clin Pharm Team.

Please send comments if you have any. I will be working from home tomorrow.

Thanks
Amna

Atkins, Brenda J

From: Johnson, John R
Sent: Thursday, June 17, 2004 2:55 PM
To: Ibrahim, Amna; Atkins, Brenda J; Dagher, Ramzi; Booth, Brian P; Ramchandani, Roshni
Subject: RE: Camptosar label

Amna

In the Special Populations section under *Pediatrics* where the PK data has been deleted I would insert. "See Pediatric Use in the Precautions section".

In the Pediatric Use section use Arabic numbers for Phase 2 instead of Roman. Otherwise OK.

John

-----Original Message-----
From: Ibrahim, Amna
Sent: Thursday, June 17, 2004 2:20 PM
To: Atkins, Brenda J; Johnson, John R; Dagher, Ramzi; Booth, Brian P; Ramchandani, Roshni
Subject: Camptosar label

<< File: Camp label-061704.doc >>
After addition of further toxicity data in the window study, I am sending this label around once more on . All changes are on page 19.

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Thanks
Amna